REMARKS

Claims 17, 21, and 22 have been amended. Claims 38-39 have been added. Support for the amendments and new claims can be found throughout the specification, including at page 2, line 22 through page 3, line 28; page 15, line 23 to page 16, line 6; and page 16, lines 16-18. Claims 23, 25, and 26 have also been amended for purposes of clarity. No new matter is added by the amendments. Claims 17, 20-23, 25-31, and 33-39 are pending in the application. Reconsideration of the claims in view of the following Remarks is respectfully requested.

35 USC § 112, second paragraph

Claims 23 and 26 were rejected under 35 USC § 112, second paragraph, as being indefinite. Regarding claim 23, the Examiner states that there is insufficient antecedent basis for "physiological saline." Claim 23 has been amended to clarify that the "hyaluronic acid is dissolved in a physiological buffer comprising physiological saline." Withdrawal of the rejection is requested.

Regarding claim 26, the Examiner states that this claim has 100% word identity to claim 25. Claim 26 has been amended to recite that the polymeric matrix comprises an unblocked polymer, while claim 25 now recites that the polymeric matrix is a blocked polymer. Withdrawal of the rejection is therefore requested.

35 USC § 102

Claims 17, 21, 25-29, and 35 were rejected under 35 USC § 102(b) as anticipated by **McGinity** et al. Applicants traverse this rejection.

Independent claims 17 and 21 as amended recite injectable formulations comprising an injection vehicle including an aggregation-reducing amount of hyaluronic acid dissolved in a physiological buffer. Applicants submit that McGinity et al. nowhere teaches or suggests an injectable formulation as claimed. Rather, McGinity et al. teaches the use of hyaluronic acid as a stabilizing agent for protein inside oil droplets of multiphase microspheres (column 27, line 61 to column 28, line 17). McGinity et al. does not teach or suggest use of hyaluronic acid in an injection vehicle.

Applicants submit that claims 17 and 21, and their dependent claims 25-29 and 35, are patentable over McGinity et al., at least for the foregoing reasons. Withdrawal of the rejection is therefore requested.

Claims 17, 21, 23, 25-29, and 34-35 were rejected under 35 USC § 102(e) as anticipated by **Cleland et al**. Applicants respectfully traverse this rejection. Independent claims 17 and 21, as amended, recite a particle formulation comprising an aggregation-reducing amount of hyaluronic acid dissolved in a physiological buffer. At column 19, lines 47-53, the reference states:

> To prepare an injection using the microspheres obtained above, the microspheres may be formulated with a viscous physiologically acceptable solution; a dispersant (e.g., surfactants such as Tween-80, HCO-60; polysaccharides such as carboxymethylcellulose, sodium alginate, sodium hyaluronate....)

The reference does not disclose or suggest an injectable formulation having an aggregation-reducing amount of hylauronic acid as claimed. Withdrawal of this rejection is therefore requested.

Claims 17, 21, 23, 25-28, and 34 were rejected under 35 USC § 102(e) as anticipated by **Suzuki** et al. Independent claims 17 and 21, as amended, recite a particle formulation comprising an aggregation-reducing amount of hyaluronic acid (HA) dissolved in a physiological buffer. Suzuki et al. does not disclose or suggest an injectable formulation as claimed, but discloses use of HA as a dispersant.

> It is particularly preferred to use a microcapsule-dispersing medium which contains one or more compounds selected from the group consisting of hyaluronic acid, chondroitin sulfate, and salts thereof. The use of such a dispersion medium makes it possible to minimize irritation to the joint, which tends to occur as a result of administration. (Suzuki, Col 5, Lines 2-8)

Withdrawal of this rejection is requested.

35 USC § 103

Claims 17, 20-21, 23, 25-29, and 34-35 were rejected under 35 USC § 103(a) as unpatentable over **Cleland** et al. in view of page T515 of the **Aldrich catalog** (1996-1997). Claim 26 has been cancelled. With regard to the remaining claims, Applicants traverse this rejection.

Independent claims 17 and 21, as amended, are traversed for the same reasons discussed above for the 35 USC § 102 rejections. Specifically, Cleland et al. neither teaches nor suggests an injectable formulation as claimed, wherein the formulation comprises an aggregation-reducing amount of hyaluronic acid. Page T515 of the Aldrich catalog simply discloses various gauge needles and does not remedy the deficiency of Cleland. Applicants respectfully submit that neither Cleland et al. nor the Aldrich catalog, alone or in combination, teach or suggest an injectable formulation as claimed. Withdrawal of the rejection is requested.

Claim 20 recites a method for injecting a particle formulation through a 23-gauge or smaller needle as claimed. The Examiner asserts that one of skill in the art would have been motivated to deliver the formulation using a syringe of 23-gauge needle as disclosed in the Aldrich catalog. Applicants respectfully disagree.

The administration of polymer-based drug formulations is known to be problematic (paragraph bridging pages 2-3 of the application). Previously, excipients, surfactants, and salts have been added to reduce agglomeration or alter the particles' fluid properties (page 2 line 26 to page 3, line 2). Nevertheless, administration of the formulations through 21 or 23 gauge needles is difficult (page 3, lines 3-4). Furthermore, the use of large-bore needles increases the pain of injection (lines 5-7).

Applicants have discovered that the use of hyaluronic acid in polymer-based formulations can allow the use of 23 gauge or smaller needles. Applicants have provided working examples demonstrating that the claimed formulations can be administered in small needles (Examples 3, 4, 5, and 7). Applicants have demonstrated that the use of hyaluronic acid in formulations for injection through smaller needles is unexpectedly superior compared to other polymers, such as sodium alginate, dextran 70, jeffamine M-600, jeffamine ED-2001, keretan sulphate, laminin, poly-L-ornithine, xanthan gum, and gellan gum (Example 6).

Consequently, in view of the known problems with the use of smaller needles to inject polymer-based drug formulations, one of skill in the art would not have been motivated to inject the claimed formulation through a 23 gauge or smaller needle, as recited by claim 20. Applicants respectfully submit, therefore, that neither Cleland et al. nor the Aldrich catalog, alone or in combination, render claim 20 obvious. Withdrawal of the rejection is therefore requested.

Claim 22 recites a specific range of HA added to the formulation. This claim was indicated allowable if rewritten in independent format. Claim 22 has been amended to independent format. Allowance is requested.

SUMMARY

Applicants submit that the claims are in condition for allowance and notification to that effect is earnestly solicited. The Examiner is invited to contact Applicants' representative if prosecution may be assisted thereby.

Respectfully submitted,

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